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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/451,641	11/30/1999	Danchen Gao	3169-FUS	9327

25590 07/03/2002

ATTN JENNIFER AMUNDSEN
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CHICAGO, IL 606805110

EXAMINER
TRAN, SUSAN T

ART UNIT	PAPER NUMBER
1615	17

DATE MAILED: 07/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office action was mailed to you on 7/3/02. However, it was returned back to us. The envelope indicated that you were no longer with the firm. Attached you will find the office action that was mailed on 7/3/02 along with a copy of the returned envelope. Please file a change of addresswith our office.

Brenda L. Gray
SLIE, TC 1600
Team 4

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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/481,641	01/30/1999	Danchen Gao	5169.1 US	9327

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EXAMINER
IRAN, SUSAN I

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 07/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary

09/451,641	Gao et al.
Examiner: Susan Tran	Art Unit: 1615

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address*

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on *Nov 6, 2001*

2a) This action is **FINAL**. 2b) X This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *1-94* is/are pending in the application.

4a) Of the above, claim(s) *51-75* is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) X Claim(s) *1-50 and 76-94* is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1. X Notice of References Cited (PTO-892)
2. Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. X Information Disclosure Statement(s) (PTO-1449) Paper No(s). *16*
4. Interview Summary (PTO-413) Paper No(s).
5. Notice of Informal Patent Application (PTO-152)
6. Other:

DETAILED ACTION

Receipt is acknowledged of applicant's Information Disclosure Statement filed 11 06 01, Supplemental Information Disclosure Statement filed 05 02 02, Amendment C filed 11 06 01, and Request for Continued Examination filed 11/06/01.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/06/01 has been entered.

Claim Rejections - 35 U.S.C. § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Black EP 0 863 134 ('134).

Black teaches a compound useful as a Cox-2 inhibitor for pain relief, fever and inflammation of a variety symptoms disclosed on page 3, lines 29-36. The compound can be administered orally in the form of tablets, troches, lozenges, or capsules (page 4, lines 1-12). The tablets comprising active ingredient in admixture with excipients, i.e, diluents, disintegrants, binding agents, wetting agents, and surfactant (page 4, lines 15-38). The active agent present in an amount of 10 to 250 mg, and carrier material may vary from about 5 to about 95% (page 5, lines 39-58). The dosage can be administered once or twice a day, and will provide effective $T_{1/2}$ over a 24 hours period (page 5, lines 22-27). Example 2 discloses the amount of excipients use in a tablet.

The examiner notes that the reference is silent as to the teaching of celecoxib. However, it is the position of the examiner that celecoxib is a known selective Cox-2 inhibitor, and therefore, it would have been prima facie obvious for one of the ordinary skill in this art to, by routine experimentation determine suitable Cox-2 inhibitor to treat cyclooxygenase-2 mediated diseases. The expected result would be a suitable Cox-2 inhibitor composition having long half-life useful for the treatment of cyclooxygenase-2 diseases.

3. Claims 1-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Black, and Jain et al. US 6,165,506 in view of Plachetka et al. US 6,077,539.

Black is relied upon for the reason stated above. Although Black teaches the use of wetting agent, and dispersing agent, the reference is silent as to the teaching of bioavailability.

Jain teaches compositions comprising poorly water-soluble drug, such as NSAID (columns 1-2). The compositions further comprising wetting agent to increase dissolution rates of the solid dose (column 4, lines 54-62). Jain does not teach the claimed percentage of bioavailability of the active agent.

Plachetka teaches compositions comprising NSAID as active agent, and wetting agent (column 5, lines 35-55). The composition is shown to have long half-life, and a bioavailability of 95% (column 9, lines 35-40). Hence, it would have been prima facie obvious for one of ordinary skill in the art to modify Black's composition with the teachings of Jain and Plachetka, because the references teach the advantageous results in the use of wetting agent to increase dissolution of solid particulate drug. The expected result would be a suitable selective COX-2 inhibitor composition having fast dissolution rate and high bioavailability.

4. Claims 76-94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Black, and Plachetka et al., and Liversidge et al. US 5,552,160.

Black and Plachetka are relied upon for the reasons stated above. The references are silent as to the teaching of the process of reducing the particle size.

Liversidge teaches composition comprising NSAID, and process of preparing same (see abstract). The NSAID particle is preferably having size less than 100 μm (column 4, lines 45-54). The process of reducing the particle size is by milling using suitable mills includes high shear media mill (column 4, lines 55 through column 7, lines 1-16). Thus, it would have been

prima facie obvious for one of ordinary skill in the art to prepare the composition of Black and Plachetka, using the process of Liversidge, because it is well known in pharmaceutical art that dissolution rate can be improved by decreasing particle size.

The examiner notes that the cited references do not teach the cooling using liquid nitrogen. However, it is also well known in pharmaceutical art to use liquid nitrogen to cool any hot mixture to obtain room temperature.

Response to Arguments

5. Applicant's arguments filed 11/06/01 have been fully considered but they are not persuasive. The Examiner maintains the original 103(a) rejection.

Applicant argues that Black does not teach a relative bioavailability not less than about 50%. However, applicant's specification page 48, lines 15-16 discloses, co-precipitating the celecoxib with a wetting agent (composition C) increased the bioavailability of celecoxib. Black teaches a compound useful as a Cox-2 inhibitor in the form of powders, granules, tablets, troches, suspensions, or emulsions for pain relief, fever and inflammation. The composition comprises carriers, diluents, excipients, surfactant, dispersing agent, and wetting agent in an amount falls within the claimed ranges. Because Cox-2 inhibitor is poorly water soluble drug, therefore, wetting agent and/or dispersing agent are added to increase solubility. It is known in pharmaceutical art that increasing solubility will increase in bioavailability (also disclosed by Ansel, page 61, second column, lines 1-10). Since Black obtained the same result desired by the

applicant, e.g., controlled release, or sustained release composition having the half-live over 24 hour period, it is the position of the examiner that, prima facie case of obviousness has been shown. In absent of unexpected result, the burden is shifted to applicant to establish that the powder or granule formulation of Black does not have the bioavailability rate of 50% or more. If the initial burden on the Office to establish a prima facie case is met, the burden of coming forward with evidence or argument shifted to the applicant. *In re Oetiker*, see also *Fregeau v. Mossinghoff*, 776 F2.d 1034, 227 USPQ 848 (Fed. Cir. 1985). The burden is shifted to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility." In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995) (citing In re Bundy, 642 F.2d 430, 433, 209 USPQ 48, 51 (CCPA 1981)). *In re Brana*, the court pointed out that the purpose of treating cancer with chemical compounds does not suggest, per se, an incredible utility. Where the prior art disclosed "*structurally similar compounds to those claimed by applicants which have been proven in vivo to be effective as chemotherapeutic agents against various tumor models . . ., one skilled in the art would be without basis to reasonably doubt applicants'asserted utility on its face*." 51 F.3d at 1566, 34 USPQ2d at 1441.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Tran whose telephone number is (703) 306-5816. The examiner can normally be reached on Monday through Thursday from 600 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600